National Institute of Allergy and Infectious Diseases

PROFILE

Fiscal Year 2004

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

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This is a stylized representation of an antibody, a protein made by the body's immune system cells to protect it against invading foreign substances.

INTRODUCTION

The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases. For more than 50 years, NIAID research has led to new therapies, vaccines, diagnostic tests, and other technologies that have improved the health of millions of people in the United States and around the world. The scope of the NIAID research portfolio has expanded considerably in recent years in response to new challenges such as bioterrorism; emerging and re-emerging infectious diseases, including acquired immunodeficiency syndrome (AIDS), influenza, severe acute respiratory syndrome (SARS), West Nile virus, malaria, and tuberculosis; and the increase in asthma prevalence among children in this country. The growth of NIAID programs also has been driven by unprecedented scientific opportunities in the core NIAID scientific disciplines of microbiology, immunology, and infectious diseases. Advances in these key fields have led to a better understanding of the human immune system and the mechanisms of infectious and immune-mediated diseases.

The threat of bioterrorism has created new challenges for medicine and public health. Our Nation's ability to detect and respond to acts of bioterror requires new and improved countermeasures, including diagnostics, vaccines, and therapies. The development of countermeasures is driven by biomedical research on dangerous, disease-causing microbes and on the immune system response to these pathogens. The National Institutes of Health (NIH) and NIAID support much of this research. As the lead agency at NIH for infectious diseases and immunology research, NIAID has set research priorities and goals for each microorganism or toxin that might be used as an agent of bioterrorism, with particular emphasis on "Category A" agents—those considered to be the worst bioterror threats. NIAID's biodefense program includes both short- and long-term research targeted at the design, development, and evaluation of the specific public health tools or countermeasures needed to control a bioterrorist-caused outbreak. NIAID's advances in biodefense research are discussed in the *NIAID Biodefense Research Agenda for CDC Category A Agents Progress Report* and the *NIAID Biodefense Research Agenda for Category B and C Priority Pathogens Progress Report*.

We anticipate that the large investment in research on biodefense will provide new insights relevant to other diseases. NIAID research on microbial biology and on the pathogenesis of organisms with bioterror potential will lead to a better understanding of other more common and naturally occurring infectious diseases that afflict people here and abroad. In particular, the advancement of knowledge should have an enormous positive impact on our ability to diagnose, treat, and prevent major infectious killers, such as malaria, tuberculosis, human immunodeficiency virus (HIV)/AIDS, and a spectrum of emerging and re-emerging diseases, such as West Nile virus, dengue, influenza, and multidrug-resistant microbes. Furthermore, and importantly, the NIAID biodefense research agenda promises to enhance our understanding of the molecular and cellular mechanisms of innate immunity and its relationship to adaptive immunity. Such knowledge will help in the search for new ways to treat and prevent a variety of immune-mediated diseases, such as systemic lupus erythematosus, type 1 diabetes, and rheumatoid arthritis. New insights into the mechanisms of regulation of the human immune system also will have positive spinoffs for diseases such as cancer, immune-mediated neurological diseases, and allergic and hypersensitivity diseases, as well as for the prevention of rejection of transplanted organs, cells, and tissues.

Vaccine research has long been a cornerstone of NIAID research. Effective vaccines have

contributed enormously to improvements in public health worldwide, and research supported by NIAID has led to new or improved vaccines for a variety of serious diseases, including rabies, meningitis, whooping cough, hepatitis A and B, chickenpox, and pneumococcal pneumonia. NIAID has three broad goals in vaccine research: identifying new vaccine candidates to prevent diseases for which no vaccines currently exist, improving the safety and efficacy of existing vaccines, and designing novel vaccine approaches such as new vectors and adjuvants.

One of the important challenges for the 21st century is the development of safe and effective vaccines for the three greatest microbial killers worldwide: HIV/AIDS, malaria, and tuberculosis. These three diseases account for one-third to one-half of healthy years lost in less-developed countries. NIAID has a robust portfolio of vaccine research and development for these and other diseases of global importance, including those caused by agents of bioterrorism. Another important focus is the development of next-generation influenza vaccines made with modern technologies that improve on the current egg-based method of production. Significant progress has been made in developing new vaccine candidates against both "interpandemic" flu strains that currently are circulating among humans, as well as strains with pandemic potential, such the H5N1 avian influenza seen in humans in Southeast Asia.

Despite recent progress in treatment and prevention, HIV disease and AIDS continue to exact an enormous toll throughout the world. Estimates on the scope of the HIV/AIDS pandemic are profoundly sobering. An estimated 39 million people worldwide are living with HIV/AIDS, and approximately 11 of every 1,000 adults aged 15 to 49 are HIV-infected. In 2004 alone, HIV/AIDS-associated illnesses caused the deaths of approximately 3.1 million people worldwide. More than 95 percent of these infections and deaths have occurred in developing countries, most of which also are burdened by other significant health challenges.[1] To help turn the tide of the global HIV/AIDS pandemic, NIAID has established research collaborations with international colleagues in more than 50 countries to develop comprehensive approaches to the HIV pandemic, encompassing vaccine development and other prevention activities, therapeutics, and care of the HIV-infected person. These collaborations already have yielded important results, notably in developing methods to reduce mother-to-child transmission of HIV.

NIAID-sponsored researchers have made critical discoveries about the basic biology of HIV and the immune response to HIV infection, which in turn have led to the development of therapies that suppress the growth of the virus in the body. Although much has been learned in recent years, questions remain about the molecular interactions involved in the regulation of HIV expression and replication, why the host immune response fails to control the infection, and how reservoirs of virus persist in the body despite highly active antiretroviral treatment (HAART). NIAID continues to search for more scientific information about how the virus attacks the body and how the body defends itself, both of which are critical for identifying additional targets for therapeutic interventions and vaccines.

An important NIAID research focus is the immune system, the complex network of cells, tissues, and organs that work together to defend the body against attacks by foreign invaders such as bacteria, viruses, parasites, and fungi. Because the human body provides an ideal environment for many microbes, they try to break in. It is the immune system's job to keep them out or, failing that, to seek out and destroy them. When the immune system hits the wrong target or is crippled, however, many diseases may result, including asthma and allergy diseases, arthritis, or AIDS. NIAID-funded research in basic and clinical immunology has led to many promising approaches for treating individuals

with immunologic conditions such as multiple sclerosis, type 1 diabetes, and asthma. For example, researchers are developing novel ways to selectively block inappropriate or destructive immune responses while leaving protective immune responses intact, an area of research known as tolerance induction. The NIAID-supported Immune Tolerance Network (ITN) is an international consortium of approximately 80 basic and clinical scientists and physicians at more than 40 institutions in the United States, Canada, Europe, and Australia. ITN has 18 approved clinical protocols that are enrolling patients, or will do so soon, in areas such as islet transplantation for type 1 diabetes, kidney transplantation, autoimmune diseases, and asthma and allergic diseases. In September 2004, NIAID launched a three-site consortium that will work to improve the outcomes of organ transplantation. The percentage of patients who live for a year after an organ transplant has risen dramatically over the past 15 years, but there has been only modest success in improving the odds of long-term survival. This research consortium will move us closer to minimizing the debilitating and sometimes fatal complications of organ transplantation.[2]

For the past decade, NIAID also has focused on reducing the significant and growing burden of asthma among inner-city minority children. NIAID's Inner-City Asthma Study has investigated novel interventions to improve the health of inner-city children with asthma. One approach, called a physician feedback intervention, involves periodic reports to the child's doctor about the status of the child's asthma. These reports, generated from bimonthly phone interviews with parents, recommend changes in the child's treatment regimen according to National Heart, Lung, and Blood Institute guidelines, if warranted. Another method involves an environmental intervention to identify and remove asthma triggers, such as cigarette smoke or cockroaches, from the child's home. Both interventions are reducing healthcare utilization, and the children receiving the environmental intervention gained an additional 3 weeks of symptom-free days during the intervention year. We are working to make such interventions available nationwide.

Profile describes the Institute's activities in areas of basic research and clinical investigation and provides overviews of the major accomplishments and goals of the various scientific programs within the Institute. *Profile* also includes information on the organization and staff of NIAID, the Institute's budget, and its extramural grants, contracts, and research training programs.

We still have much to discover about many infectious and immune-mediated diseases and how best to diagnose, treat, and prevent them. However, with a strong research base, talented investigators in the United States and abroad, and the availability of powerful new research tools, we fully expect that our basic and applied research programs will provide the essential elements to enhance our defenses against those who would attempt to harm us with bioterrorism, to develop new tools in the fights against HIV/AIDS and other infectious diseases, and to improve therapies and management of immune-mediated diseases.

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[1] UNAIDS. AIDS epidemic update: 2004. Available at *http://www.unaids.org/wad2004/report.html*.

[2] NIAID Forms Clinical Consortium to Improve Success of Organ Transplants. *NIH News*, Sept. 13, 2004. Available at: *www.niaid.nih.gov/Newsroom/Releases/organtrans.html*.